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A NOTE ON THE ASSAY OF THE HALOGEN COMPOUNDS OF THE U. S. PHARMACOPŒIA, WITH SPECIAL REFERENCE TO THYMOL IODIDE.

By Elias Elvove.

In connection with an investigation on the relative bactericidal value of the various embalming fluids on the market, which is now in progress in the Division of Pathology and Bacteriology of the Hygienic Laboratory, it was required, among other things, to examine a number of these fluids for the presence of chloral and to estimate its quantity wherever found. Owing to the more or less complex nature of these fluids and especially to the fact that nearly all of them contain comparatively large amounts of formaldehyde, the methods for estimating chloral, such as those given by Allen, Holland, or Schimpf, are inapplicable to these fluids. Thus Allen[1] gives the processes of Müller,[2] Wood,[3] and Meyer,[4] all of which depend on the reaction of chloral with alkalies with the separation of chloroform and measuring the volume of the latter. The smallest of the quantities of chloral operated on is 1 or 2 grammes (Meyer), while in the method of Wood 10 grammes are used, and in the method of Müller 25 grammes. In cases such as the embalming fluids under consideration, where we may be dealing with comparatively small quantities of chloral, this circumstance alone would bar consideration of any method which

[1] Allen: Commercial Organic Analysis, 3rd ed., Vol 1, pp. 229–230.
[2] *Zeit. f. Chem.*, (2), **7**, 66, and *Jour. Chem. Soc.*, **24**, 444.
[3] *Pharm. Jour.*, (3), **1**, 703.
[4] Meyer (and Haffter): *Ber.*, **6**, 600–601, and *Jour. Chem. Soc.*, **26**, 1163.

is based on measuring the volume of chloroform produced. According to Holland,[5] chloral is estimated by adding a measured amount of $\frac{N}{1}$ NaOH to render the solution distinctly alkaline and determining the excess of alkali (Meyer's method). Schimpf[6] gives essentially the same method, but also includes the iodometric method of Rupp.[7] However, neither the alkalimetric nor the iodometric method is applicable to the estimation of chloral in the embalming fluids on account of the simultaneous presence of formaldehyde.

Fortunately, the fact that chloral contains chlorine, which can be converted into a chloride, affords a simple and convenient basis for indirectly estimating the amount of chloral. Procedures for decomposing the organic molecule so as to obtain its chlorine in the form of chloride are given by many authors under chloroform, but under chloral preference appears to be given to some form of the alkalimetric method, while a number of authors even omit any reference to the chloride process in the latter case. That such preference is not justifiable, however, may be seen from the work of Hinrichs,[8] who has pointed out the gross errors (varying from 180 to 200 per cent.) resulting from the alkalimetric procedure when the term "heating," as used by the British Pharmacopœia, is taken to mean warming till all the odor of chloroform has disappeared. Hinrichs, therefore, describes a modification of that method which, however, still does not make it suitable in the case of the embalming fluids; so that for general analytical purposes the chloride method is probably the best of all.

This chloride method may be carried out according to either the procedure of Wallis[9] or that of Self.[10] The essential feature of Wallis' procedure is the decomposition of the chloral by heating with an alcoholic solution of alkali under pressure, which is effected by heating the mixture in a closed bottle by means of boiling water for three hours. This is, therefore, practically the same procedure as that previously described by Puckner[11] for the estimation of chloroform. In Self's method the decomposition of the chloral is effected by boiling the solution containing the chloral with zinc

[5] Holland: Medical Chemistry and Toxicology, 2d ed., p. 412 (1908).
[6] Schimpf: Manual of Volumetric Analysis, 5th ed., pp. 647–8 (1909).
[7] *Arch. Pharm.*, **241**, 326–8 (1903), and *Jour. Chem. Soc.*, **84**, (2), 699 (1903).
[8] *Pharm. Jour.*, (4), **16**, 530–532 (1903).
[9] *Pharm. Jour.*, (4), **22**, 162–163 (1906).
[10] *Pharm. Jour.*, (4), **25**, 4–7 (1907).
[11] Proc. A. Ph. A., **49**, 294–297 (1901).

dust under a reflux condenser, the zinc dust being replaceable by zinc filings and acetic acid, or by aluminium powder and acetic acid, the time required for effecting the decomposition of the chloral in Self's procedure being only from twenty to thirty minutes.

In this connection it seemed to the writer that having such excellent methods for estimating chloral and chloroform, it would be desirable that the U. S. Pharmacopœia (which at present gives no method whatever for estimating the percentage purity of these substances, although in the case of chloroform it prescribes a purity of 99 to 99.4 per cent.) should include, in the next revision, methods of assay based on these principles. Such want should be filled not only for the sake of consistency and completeness, but also because there is actual demand for such methods, as may be seen from the fact that the British Pharmacopœia had included a method for assaying chloral hydrate even before either Wallis or Self described their improved (chloride) methods and although the B.P. procedure, as already mentioned above, was shown by Hinrichs to be very far from satisfactory. Similarly, Gane and Webster [12] cite a controversy with one of the large users of iodoform as showing the importance of establishing a standard method of assay for this substance and point out that Utz's [13] method might be used, wherein the iodine of the iodoform is converted into silver iodide and the excess silver nitrate determined volumetrically. Likewise, in the case of bromoform (for which the present U.S.P. prescribes a purity of 99 per cent. without, however, giving any method of assay), Richaud [14] has pointed out how its bromine can be readily converted into bromide and the bromoform thus estimated through a determination of the resulting bromide. In other words, there appears no sufficient reason why a number of the halogen-containing substances of the U.S.P. should remain without any method of assay when it is quite probable that every one of them could be very readily estimated through a determination of its halogen. Further, it is quite probable that the conversion of the organic halogen into inorganic halide can be effected in all cases by some modification of the alkaline or of the reduction method (typified by the Wallis and Self procedures, respectively,

[12] *Pharm. Jour.*, (4), **28**, 555 (1909).
[13] *Apoth. Zeit.* (Berlin), **18**, 869 (1903).
[14] *Jour. de pharm. et de chim.*, (6), **9**, 232–236 (1899), and *Jour. Chem. Soc.*, **76**, (2), 527 (1899).

in the case of chloral) or through a suitable combination of these. The basis of all these assays would be the Volhard method, which is already in the U.S.P., but which is not fully utilized even where it is directly applicable. Moreover, the Volhard method might be applied to a number of other U.S.P. substances by previously introducing halogen into them, as was pointed out by the writer [15] in the case of a large number of the alkaloids. It will be seen, therefore, that while we would thus supply methods of assay where none are given at present, we would at the same time not increase the requirements for analytical skill on the part of the pharmacist, but simply extend the usefulness of a well-known method (the Volhard method) which is very easily carried out and which might be made to cover a very large portion of the U.S.P. field.

It appeared from the literature examined that thymol iodide, $(C_6H_2.CH_3.C_3H_7.OI)_2$, is especially difficult to decompose by a wet process so as to convert its halogen quantitatively into inorganic (or readily ionized) iodide. Thus according to Gane and Webster [16] "none of the usual wet methods is applicable; only partial decomposition is effected by heating with alcoholic potash to 130° C. under pressure, while neither treatment with silver nitrate and nitric acid nor with freshly precipitated silver chloride is suitable." Owing to this, "resort was therefore had to fusion with alkali carbonates." To carry out such fusion, 1 Gm. of the thymol iodide is intimately mixed with an equal amount of $KNaC_4H_4O_6$ and 5 Gms. anhydrous Na_2CO_3. A porcelain crucible of 30 c.c. capacity is used, and a mixture of 1 Gm. $KNaC_4H_4O_6$ and 5 Gms. anhydrous Na_2CO_3 is employed to cover the mixture containing the thymol iodide. It is directed to "heat to such temperature as will ensure production of a perfectly white fused mass in forty-five minutes." After cooling, "thoroughly extract the fused mass with water," filter, and determine the halogen in the filtrate. As stated by these authors, resort was had to the fusion method only after finding the usual wet methods unsuitable. Inasmuch, however, as Gane and Webster apparently had not tried the reduction method, it was thought desirable to make some trials with the latter method. The following experiments were therefore carried out.

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[15] Bull. No. 54, Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv., Wash., and *Jour. Amer. Chem. Soc.*, **32**, 132–139 (1910).

[16] *Drug Topics*, **24**, 52–53 (1909).

GENERAL MODE OF PROCEDURE.

As a result of some preliminary experiments, it was found that the following procedure yielded satisfactory results: The thymol iodide[17] (0.1 to 0.5 Gm.) was treated, in a 500 c.c. Erlenmeyer flask, with 10 c.c. of ether (U.S.P.), followed by 20 c.c. of approximately $\frac{N}{2}$ alcoholic[18] sodium hydroxide and 2 Gms. zinc dust,[19] mixing thoroughly after adding each of these constituents. The contents of the flask were then actively boiled under a reflux condenser for one hour. The flask was then disconnected from the condenser and the contents acidified with 10 c.c. of glacial acetic acid (99.5 per cent.) and diluted with 200 c.c. of distilled water, mixing thoroughly after adding each of these constituents. The contents of the flask were then again actively boiled under the reflux condenser for another hour. (With this procedure there is the fortunate circumstance that the undissolved residue tends to conglomerate, while the liquid finally becomes perfectly clear and hence filters very rapidly.) The condenser was then washed with a small amount (about 10 c.c.) of water which was allowed to drain into the flask and the contents of the latter filtered (using about 30 c.c. of hot water in the washings). The filtrate then received a measured amount of $\frac{N}{10}$ $AgNO_3$ which was a little (about 5 c.c.) in excess of that theoretically required. The whole was then actively boiled for ten minutes, 50 c.c. of dilute (10 per cent.) nitric acid added, and again actively boiled for five minutes. After filtering (using about 30 c.c. of hot water in the washings) and cooling to room-temperature, the excess silver in the filtrate was determined by means of standard thiocyanate, using 5 c.c. of 10 per cent. ferric alum as indicator.

In applying the above method to assaying thymol iodide, it should also be possible to determine any considerable amount of chlorine, if present, by weighing the silver precipitate and finding the amount of chlorine by calculation as pointed out by Gane and Webster.[20]

In order to determine the effect of varying the time of the

[17] The thymol iodide used in this work was obtained from a well-known firm whose products usually are of a high degree of purity.

[18] Prepared by dissolving 20 Gms. of NaOH in 40 c.c. water and making up to 1000 c.c. with alcohol (U.S.P.).

[19] As zinc dust frequently contains small amounts of chlorine suitable controls were made in all cases.

[20] *Loc. cit.*

alkaline or the acid boiling, experiments were carried out in which the boiling time of one remained constant (one hour), while the boiling time of the other varied (up to three hours). The results obtained are given in the accompanying tables.

TABLE I

Effect of Varying the Time of the Acid Boiling

No. of experiment	Amount of thymol iodide	Time of alkaline boiling	Time of acid boiling	$\frac{N}{10}AgNO_3$ required	Apparent iodine content
	Gm.	*Min.*	*Min.*	*c.c.*	*Percent.*
1	0.3	60	15	10.62	44.93
2	0.3	60	30	10.68	45.18
3	0.3	60	45	10.70	45.27
4	0.3	60	60	10.58	44.76
5	0.3	60	120	10.70	45.27
6	0.3	60	180	10.70	45.27

TABLE II

Effect of Varying the Time of the Alkaline Boiling

No. of experiment	Amount of thymol iodide	Time of alkaline boiling	Time of acid boiling	$\frac{N}{10}AgNO_3$ required	Apparent iodine content
	Gm.	*Min.*	*Min.*	*c.c.*	*Percent.*
1	0.3	0	60	5.35	22.63
2	0.3	15	60	10.00	42.31
3	0.3	30	60	10.52	44.51
4	0.3	45	60	10.70	45.27
5	0.3	60	60	10.65	45.06
6	0.3	120	60	10.72	45.35
7	0.3	180	60	10.77	45.56

TABLE III

Effect of Varying the Amount of Thymol Iodide

Time of alkaline boiling: One hour.
Time of acid boiling: One hour.

No. of experiment	Amount of thymol iodide	$\frac{N}{10}AgNO_3$ required	Apparent iodine content
	Gm.	*c.c.*	*Percent.*
1	0.1	3.57	45.31
2	0.2	7.15	45.37
3	0.3	10.60	44.85
4	0.4	14.35	45.53
5	0.5	17.87	45.36

Percentage of iodine in thymol iodide, according to U.S.P..... 45.00
Apparent iodine content as found by fusion method (similar to that of Gane and Webster)..... 44.52

The following result was obtained by the above-described procedure in working with an ether-alcoholic sodium hydroxide mixture containing some of the thymol iodide used in this work, the amount of which was unknown to the writer at the time of working with it, having been prepared by Dr. Norman Roberts of this laboratory and submitted to the writer as an "unknown."

Amount of thymol iodide given	$\frac{N}{10}$ $AgNO_3$ found to require	$\frac{N}{10}$ $AgNO_3$ as calculated[21]	Apparent iodine content
Gm.	*c.c.*	*c.c.*	*Percent.*
0.4751	16.88	16.95	45.09

From these results it would seem that a period of one hour for the alkaline boiling and another hour for the acid boiling should be sufficient for most practical purposes even when employing as much as 0.5 Gm. of the thymol iodide, which appears to be a suitable amount to take for the assay.

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[21] This calculation is based on the average value of the thymol iodide in terms of the $\frac{N}{10}$ $AgNO_3$ as shown by the results given in Table III.

ERGOXANTHEÏN.

ERGOXANTHEÏN, A NEW ACTIVE PRINCIPLE FOUND IN ERGOT, WITH A BRIEF HISTORICAL SUMMARY OF THE DISCOVERY OF THE ALKALOIDS OF ERGOT.

By W. T. Wenzell.

The writer has nothing further to announce on the alkaloids ecboline and ergotine, the discovery of which has been duly credited and confirmed by numerous investigators at home and abroad. Their discovery was announced in this Journal in 1864 (Am. Journ. Pharm.).

However, the priority as to the naming of these alkaloids has been ignored by Kobert, in 1884, in changing the name of ecboline to coruntine, by Barger, in (1907) changing it to ergotoxine, and by Tanret, in 1875, ergotine to ergotinine. Ecboline, the name selected by the writer, is from the Greek word *εκβολπ*, the literal translation of which is "to throw out," or expel. No word could have been better chosen or adapted, on account of the physiological action of this alkaloid, the producer of the tonic contraction of the uterus.

Barger and Dale make the statement in their publication (Ergotoxine and Constituents of Ergot) as a matter of fact that ergotoxine (ecboline) in intact pregnancy of cats, as well as post-partem cases, causes uterine contractions.

Kobert admitted that ecboline and coruntine were identical (Ueber die Bestandtheile and Wirkungen des Mutterkorns 1884, p. 46), but said that it was a very impure substance or preparation of his alkaloid, which he obtained by shaking out of alkaline solutions by acetic ether.

(I make this statement that Dragendorff's method of extraction of organic principles from immiscible liquids by ether was not known in 1864.)

Kobert also changed the name of sclerotinic acid, another constituent of ergot, discovered by Dragendorff and Podwyssotzki (1876), into ergotinic acid, and the only reason he gave for making this change was that his ergotinic acid was the purer.

Usually, claims of priority of discovery rest with the discoverer, and such rights should be respected.

"Honor to whom honor is due" and much honor is also un-

questionably due to Kobert, Barger, Dale, and others, for the amount of labor bestowed to obtain the valuable results in elucidating the chemistry and physiologic action of the active constituents of ergot.

The writer, herewith, announces an active constituent found in the fluidextract of ergot, not an alkaloid, but a principle possessing an undoubted action upon the human organism. This substance has been provisionally named ergoxantheïn (ergot-yellow) on account of the color of its alcoholic and etherial solutions.

THE PREPARATION OF ERGOXANTHEÏN.

Twenty-five cubic centimetres of Squibb's fluidextract were mixed with 75 c.c. of 95 per cent. alcohol, the mixture allowed to stand, with occasional shaking, about 12 hours. A dark brown precipitate will separate out, the clear supernatant liquid acquiring a sherry-wine color.

The precipitate is composed principally of Dragendorff's scleromucin, a violet coloring matter probably scleroxanthin, a resin, and magnesium, potassium, and iron salts of phosphoric acid.

The filtrate from this precipitate was evaporated in a shallow dish at a temperature of about 30° C. until the alcohol was completely expelled, adding from time to time water. Then diluted with water to measure 50 c.c., allowed the mixture to cool, and the dark brown precipitate to settle. Next transferred the mixture to a filter, collected the precipitate and washed it with water until 100 c.c. of filtrate were obtained. This brown precipitate represents the impure sphacelic acid of Kobert mixed with separated carbon.

The filtrate from this precipitate was then transferred to a stoppered separator, mixed with an equal volume of chloroform, and well shaken together, in order to remove a resinous substance. The filtrate having been shaken out thoroughly by chloroform was next mixed with an equal volume of ether and shaken until the etherial extraction became nearly colorless.

The shaking out in each case should be continued at least three times. The mixed etherial yellow extraction which now holds the ergoxantheïn in solution was distilled from a Liebig's condenser to a small volume, transferred to a small tared beaker, the liquid finally evaporated on a water bath to dryness and weighed. The amount of ergoxantheïn usually obtained will average about 0.25 per cent.

This solid residue when dissolved in 25 c.c. of alcohol will constitute the standard solution, representing 25 c.c. of the fluidextract, to be used in the physiologic and spectroscopic experiments.

PHYSICAL AND CHEMICAL PROPERTIES.

Ergoxantheïn presents an orange-yellow, uncrystallizable solid. It is soluble in alcohol and ether, but insoluble in water and chloroform. Its alcoholic solution does not redden blue litmus paper. It combines with alkaline bases forming blood-red solutions, alcoholic or aqueous.

Ergoxantheïn seems to bear a close relationship to luteïn, a yellow resinous pigment distributed in the vegetable and animal kingdom. Luteïn is a constituent of the ray-fungus, the spectrum of which is almost identical with that of ergoxantheïn, but it differs materially in its behavior towards chemical tests.

When solid ergoxantheïn is brought in contact with strong nitric acid, its yellow color is changed to a deep orange color, while luteïn acquires a blue color. Sulphuric acid dissolves ergoxantheïn to a blood-red solution. These substances also differ in the color of their solutions in chloroform, lutein giving an orange color, while ergoxantheïn retains its yellow. Again, ergoxantheïn is very soluble in alcohol, on the other hand, luteïn is sparingly soluble and in concentrated hot solutions deposits orange flakes on cooling.

Ergoxantheïn is soluble in ether, benzene, acetic ether, amyl alcohol, acetone, and carbon disulphide. Insoluble in water, carbon terrachloride and chloroform.

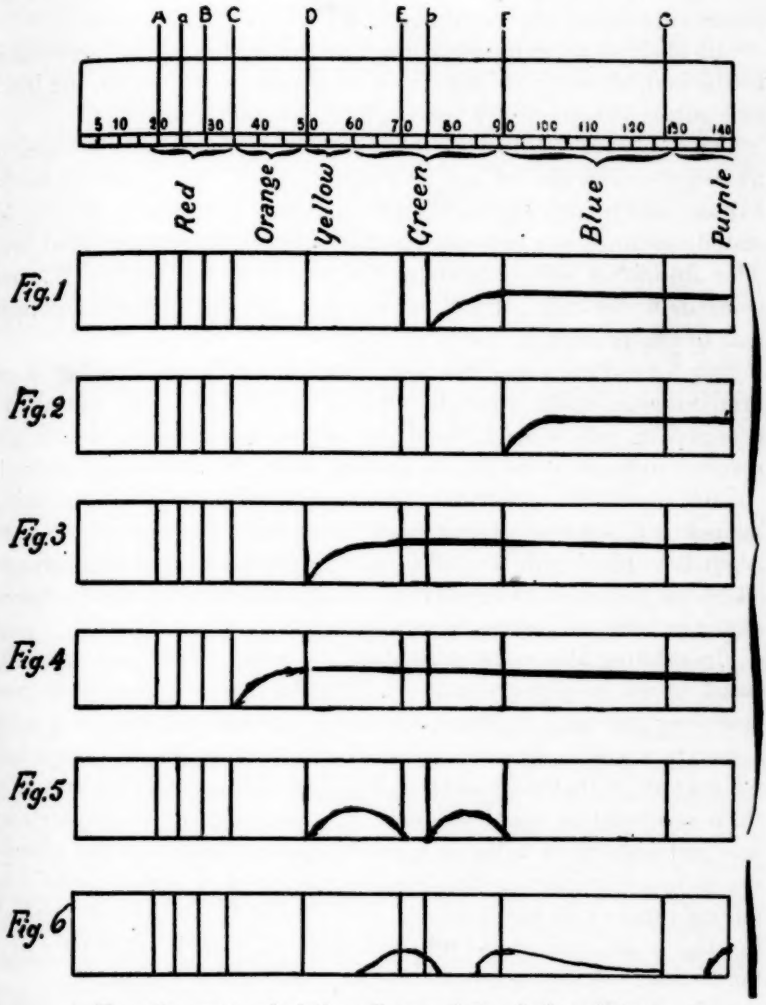
Basic lead acetate precipitates it from alcoholic solutions as an orange precipitate. It is not precipitated by barium chloride. Phosphotungstic acid precipitates ergoxantheïn yellow.

ON OTHER PIGMENTS FOUND IN ERGOT.

Zinnin, in 1853, showed that a coloring matter could be extracted from ergot by means of alcohol strongly acidulated with sulphuric acid. He recommended it for the detection of ergot in flour. But no spectrum analysis of it was made.

Uffelmann announced (*Archiv. f. Hygiene,* Jahresbericht der Pharm., 1881–82) a yellow coloring matter, which he also proposed as a test for the presence of ergot in flour, by the extraction with a weak solution of caustic soda. The red liquid which he obtained

was acidulated with hydrochloric acid which changed it to a rose color. This liquid when shaken out with ether, and this solution subjected to spectrum analysis gave the spectrum, Fig. 5.



Absorption spectra of solutions of ergoxanthein and other substances.

Wladimir Tichomirow proposed (*Pharm. Zeit. fur Rüssland,* 1865) the spectrum, shown in Fig. 6, of another pigment for the discovery of ergot in flour, as in Zinnin's case a blood-red solution

was obtained on extracting the suspected flour with alcohol, strongly acidulated with sulphuric acid. Evidently, this pigment was identical with that of Zinnin's.

Fig. 1.—This spectrum represents the absorption spectrum of lutein existing in the ray-fungus, *Actinomyces* (pathogenic).

Its absorption beginning at the Fraunhofer line b. and continuing to the end, showing an absorption of a part of the green, the blue, and purple luminous rays (strength of solution unknown).

Fig. 2.—This represents the spectrum of ergoxantheïn solution as it appears in the 25 c.c. as obtained from 25 c.c. of the fluidextract which also represents the standard solution as previously stated contained in a test-tube having an internal diameter of 10 mm. The absorption will be seen to commence at the line of F., and continue to the end. It will be seen that this absorption is less than that of the preceding.

Fig. 3.—This gives the spectrum of an alcoholic solution of ergoxantheïn made strongly alkaline with ammonia, which has changed its yellow to a blood red. This spectrum shows its absorption to begin at the D. line leaving intact the orange and the red.

Fig. 4.—This absorption spectrum represents the preceding ammoniacal solution of ergoxantheïn viewed through a 100 mm. sugar tube filled with this solution. By means of this arrangement all of the colors of the spectrum are eliminated with the exception of the red, the absorption beginning at the C. line.

In diluting this normal alkaline alcoholic solution of ergoxantheïn, in the proportion of 2 c.c. to make up 10 c.c. solution, and analyzing the same by the spectroscope through the 200 mm. tube, a spectrum will be obtained identical with that of Fig. 4. From this we may infer that the spectrum analysis of a solution of ergoxantheïn representing equal volumes of it and that of the fluidextract may not only be of value in forensic chemical analysis, but also be useful in a quantitative determination of ergot in preparations containing ergot or its fluidextract. Since by such colorimetric method, through a 200 mm. sugar tube two-fifths of a cubic centimetre of a fluidextract equal to 0.4 Gm. of ergot may thus be estimated.

Fig. 5.—The spectrum of Uffelmann's yellow coloring matter showing an absorption band between the Fraunhofer line C. and E. and another band between the line B. and F.

Fig. 6 gives the spectrum of Tichomirow's pigment which, as will be seen, differs materially from the preceding spectra. Its

appearance is that shown in dilute solutions; in concentrated solutions the absorption is complete from the D. line to the end.

In connection with this subject it should be stated that Dragendorff and Podwyssotzki's scleroxantheïn, fusco sclerotinic acid scleroerithrin, and sclerojodin belong to the analogous series of ergot pigments. They are characterized by forming color-combinations with alkalies. They are with the exception of scleroxantheïn soluble in strong alcohol only, and therefore do not appear as constituents of the official fluidextract on account of their insolubility in the menstruum used in its preparation: scleroxantheïn being the exception. As the following data will show scleroxantheïn and ergoxantheïn have nothing in common.

Scleroxantheïn is a crystalline substance. It is soluble in alcohol, and soluble in water. When its solution is treated with ferric chloride it is first colored violet, then changed to blood red.

On the other hand, ergoxantheïn is very soluble in alcohol, but insoluble in water. When its solution is treated with ferric chloride, instead of violet or red, the yellow color is changed to a dark amber.

ON THE PHYSIOLOGIC ACTION OF ERGOXANTHEÏN.

For ascertaining the action of ergoxantheïn upon the human organism the standard alcoholic solution of 25 c.c., equivalent to 25 c.c. of the fluidextract, was used. Of this solution 1 fluidrachm, equivalent to about 4 c.c., was used as a dose for determining the blood-pressure by Gaetner's Tonometre, Dr. A. W. Perry, San Fran., officiating. The pressure was recorded in millimetres taking also at the same time the pulse beats of the radial artery. The observations were made every 5 minutes. After ten minutes, the pulse dropped from 80 to 75 beats per minute. The blood-pressure at the initial point stood at 133 mm., had now risen to 168 mm. as its maximum pressure, giving an increase of 27 mm. The blood-pressure from this time on dropped to its initial within half an hour, the slowing of the blood beats during the experiment being the general law that the lowering of the pulse is inversely proportional to the blood-pressure.

The following effects were experienced by the writer during the experiment:

A sense of fulness in the head, face flushed, considerable mental exhilaration.

This experiment was repeated several times, with slightly varying results.

Additionally, it may be asked why the author selected the official fluidextract of ergot for the foregoing investigation; it may be stated, that I have been prompted by several reasons. *First,* a promise that I would present a paper to be read at the meeting of the American Pharmaceutical Association, held in Los Angeles, on the "Quantitative Estimation of the Alkaloids Ecboline, and Ergotine in the Official Fluid Extract of Ergot."

During the course of analysis, when finally the chloroform solution was evaporated spontaneously, the ergotine was found to occupy the centre of the deposit in the form of prisms, while the amorphous ecboline occupied the peripheral margin of the deposit.

In order to separate the two alkaloids by the usual solvents in which they were both readily dissolved, carbon tetrachloride seemed to dissolve ergotine in preference to ecboline, but, unfortunately, it dissolved also a portion of ecboline thus rendering the complete separation of the two alkaloids so far hopeless, and the result, for the present, must remain *in statu quo.*

Second, having at this time the fluidextract under investigation, I desired to make, also to institute, a systematic qualitative analysis of it believing that inasmuch as Squibb's fluidextract prepared by repercolation would fully represent the medicinal activity of the drug, naturally, preference was given to it.

MANUFACTURE OF MEDICINAL PLASTERS.

By Frederick B. Kilmer.

I understand that Professor Remington is authority for the statement that the spreading of plasters has, to a great extent, become a lost art to the pharmacists of this country. If this statement be accepted it may be well for a few moments to go back into history in order to obtain some information in regard to this so-called "lost art."

We are told that the art of surgery had its birth at the time when injuries of primitive man began to be bound with adhesive substances made from the gums and juices of the forest. We know that as an accompaniment to the incantations of the medicine man use was made of the poultice or plaster, which, though empirical, had

some beneficial action. From the priesthood of Isis down to the monks of the near past, we find a remarkable knowledge of gums, juices, resins, and that remedial applications of plasters, salves, and ointments were skilfully prepared therefrom. In the Materia Medica of the Aryans, we find that they gave particular attention to the preparation of ointments, salves, plasters, and poultices. The Greeks assigned a place within their temples, where plasters were spread and medicines prepared by trained pharmacists. From the writings of Moses and from Egyptology we find that the Egyptians had a skilful knowledge of gums, resins, ointments, salves, blisters, etc., and knew how to apply them. In the plaster dispensed by the Chinese pharmacist of to-day, we look upon the form of plaster in use at least as far back as the middle ages. A novel method of plaster making is of ancient Arabic origin. It seems that certain kinds of domestic wines are treated with pitch, which gives to them a decidedly smoky flavor. This wine is stored or carried about in leather bottles. In the course of time the interior of the container is coated with the deposited pitch and wine sediments. The leather bottle is then cut into plasters, which find a ready sale. Many formulas found in the pharmacopœias of the present day, including those of plasters, are modifications of similar ones which descended from Hippocrates, Herophilus, and Mantras, who lived in periods ranging from 250 to 500 years, B.C. One branch of the so-called "sects" who controlled medicine about 300 B.C. relied largely upon the use of narcotics, such as opium, conium, and hyoscyamus, in their plaster and poultice making. The well-known diachylon plaster is quite similar to one devised by Menecrates, who lived in the first year of the Christian Era. In the first authoritative guide, or pharmacopœia, viz., that of Valerius Cordus, the formulas for plasters included a large proportion of diachylon base, with which he incorporated vegetable and mineral drugs, plant juices, etc. Many of the pharmacopœial plasters of the present time are evolutions of those given by this author. As Menecrates compiled and put into intelligent form the formulas of the schools preceding him, we can believe that many of our official formulas have the merit of antiquity.

That the condition of the drug trade, especially as applied to plasters, has not greatly changed may be deduced from a memorial of the druggists of Nuremberg, in 1581, who recite, among other things, that—"Counter sales are now made by the cheap corner

grocery shops, thus robbing the druggist of a source of profit that he is justly entitled to. Ointments and plasters, which certainly belong to the exclusive field of pharmacy, are now dispensed by barbers and physicians, who are neither justified by precedent nor by qualification to handle these things."

In our own country there is evidence of an ancient and advanced civilization which existed on some parts of the continent, and among the relics of this ancient civilization are implements of pharmacy. It has been suggested that the Pueblo Indians, who are descended from the Aztecs, have from a remote time made plasters, salves, and cerates, which they sometimes spread on skins, leaves, and flexible barks, and it is believed that they knew the art of applying them in surgery.

The early colonists derived a great amount of medical knowledge from the Indians, and the gums of the new-found world were early made articles of commerce in the shape of salves, plasters, etc., which were lauded as "new discoveries" possessing miraculous virtues. Many a colonial quack gained his reputation on the supposed merits of his "wonderful healing plasters," and at times these were sent back to the old country. An early American industry, conducted by the Huguenots, was the preparation and tanning of skins for the use of the plaster makers of France.

In the early days of medical practice in this country the plasters were made in the doctor's office by the apprentice, or by members of the family of the practitioner. Colonial merchants handled in considerable quantities, plasters in sticks, rolls, and spread plasters, the mass for which was imported. These were mainly diachylon and epispastic plasters. Blister plasters were evidently popular in colonial days. In one physician's bill, noted by the writer, blister plasters were charged to the same patient twenty-six times in two months, the average price for these plasters was three shillings.

From the colonial days until about 1874, the pharmacopœial plasters were made up almost entirely with the diachylon base. There are probably pharmacists who are familiar with the once well-known names of De La Cour, Wyeth, Maxwell, Shoemaker, Ellis, Skidmore, Shivers, and Husband as plaster manufacturers. These makers produced plasters in rolls to be spread by the pharmacist, or which were spread upon kid, sheepskin, or cloth. Products of this character were in common use as late as twenty-five years ago.

The manufacture of De La Cour's adhesive plaster is associated with Philadelphia in the present generation with Joseph Carl De La Cour, a graduate of the Philadelphia College. The original maker was John Charles De La Cour, who was an apprentice in a drug store in Philadelphia. He opened a drug store in Camden as early as 1836. It is stated that at this time this was the only drug store in New Jersey, south of Bordentown. He became a manufacturer and prepared solid and liquid preparations, old-fashioned court-plaster, and a general line of pharmaceutical preparations. He was among the earliest producers of ready spread or machine spread adhesive plaster in this country; he improved the formula of what is known as De La Cour's improved adhesive plaster, which was extensively used in hospitals and in the army and navy of the United States. It also became popular in tropical countries and in these countries has a large sale to-day. The manufacture is still continued in the laboratories by the original process, under the supervision of J. Carl De La Cour.

There are probably a number remaining in the ranks of pharmacy who have a vivid recollection of plaster making as practised a little over a generation ago. Plaster spreading was directed to be done with the aid "of a peculiar iron heated by means of a spirit lamp," a process which exhausted the patience when applied to the refractory masses in the shape of official plasters.

Plasters with an India rubber base had their origin about the year 1845, when Horace Bay and Dr. Shecut invented a combination of India rubber and the gums ordinarily used in the plaster mass; this they spread in a crude way and made the plaster porous. The process used by them was to dissolve the rubber in a solvent, such as benzin, turpentine, and bisulphide of carbon, and to this they added the gums and spread the mixture with a brush on a fabric. The process was the subject of a patent, which was sold to Dr. Thomas Allcock, and the plasters known as "Allcock's Porous Plasters" originated from this effort.

Some years later a process of mixing the rubber with gums and calendering the mass on fabric was perfected by Dr. John W. Newell, a rubber manufacturer, of New Brunswick, N. J. The process was covered by patents and secrets and was not applied to pharmaceutical plasters until many years later.

Few who now use the elegant plasters found in the market

realize what a combat with difficulties there has been to bring them to their present high standard. Probably no other branch of the pharmaceutical art has been the occasion of so much toil, anxiety, and discouragement before any measure of success was met in a pharmaceutical, commercial, or therapeutic sense. The evolution of India rubber plaster making has now reached a point where it not only requires a large amount of machinery, but a vast amount of detail in every step, which only long experience and accurate judgment can give. Prominent among the names connected with plaster making are those of Dr. Grovenor, of Boston, Mass., the late George J. Seabury, and the late Robert W. Johnson, of Johnson & Johnson, New Brunswick, N. J. It is to these men that we are indebted for the idea of making pharmaceutical plasters with a rubber base and for the great benefits which have accrued to medicine and surgery through the improvement in the art.

These manufacturers first used what is known as the benzin process. After considerable struggling they found that many of the medicaments of the Pharmacopœia were not compatible with rubber dissolved in a solvent, and the products were not fitted for therapeutic use and were worthless commercially. Benzin plasters are still made, but they rapidly decompose and many pharmacopœial drugs are useless in such a combination.

The pioneers in India rubber plaster making found that mechanical troubles were not all that were to be overcome, and it was only after a long struggle that the point was reached where the required pharmaceutical combination could be made and marketed in the shape of India rubber plasters, and it was not until a few years ago that it was recognized that a plaster was valueless to medicine and pharmacy if only the mechanical perfection was considered, without regard to the therapeutic efficiency and certain other requirements. It was, therefore, determined that mechanically the plasters should be made perfect and above all that the medication should be absorbed by the integument and thus make the plaster not only a mechanical application, but a therapeutic agent.

These conditions have not yet been completely fulfilled. It is undoubtedly true that rubber base plasters are superior as therapeutic agents to those made with a resin or diachylon base, and the rubber base plasters have been improved in such a way as to

render action of the medicinal agents contained therein possible. From a therapeutic point of view it seems to be true that a rubber base plaster will, under some conditions, promote, and under other conditions hinder, absorption.

Attempts have been made from time to time to produce excipients which would soften the base, also to add mild detergents which would soften the epidermis and thus assist in promoting absorption. Some years ago a special line of dermal plasters was offered, where a large amount of drug was held in perfect contact with the diseased skin, forming a vapor chamber.

I do not think that the plaster makers' art has anywhere nearly reached its limit, we are still looking for the ideal plaster mass. We need a compound of the peculiar nature of our present mass-elastic, adhesive at body temperature, easy of removal, but which will, in addition to the properties of the present mass, have a softening effect upon the skin. It would be desirable to have a mass which could be compounded with a more extended range of medicines. The present rubber mass will not admit of the use of many desirable combinations; for example, certain metals, such as lead, copper, iron, etc., cannot be compounded with the rubber mass. India rubber mass plasters are useless when the medicament is a free alkaloid. Oils and fats are to a limited extent only useful in the rubber combination.

The advantages of India rubber plaster mass, both for adhesive plasters and for medicated plasters, are well known. They have been summarized as follows: Purified rubber is a neutral element, and especially valuable as a vehicle for plasters on account of its great elasticity and flexibility. India rubber preserves the incorporated medicaments from evaporation and from decomposition. India rubber is highly resistant to moisture and to atmospheric influences. It has been stated by well-known therapeutists that a medicament properly combined with adhesive agents containing rubber, gives increased local action of the incorporated drug.

India rubber plasters adhere closely to the skin; they adhere at the temperature of the body without added heat or moisture. They are perfectly pliable at any temperature, and when once applied they do not slip or move, and they remain serviceable longer than any other form of plaster mass. This latter statement is undoubtedly true. Those who are familiar with the rapid decomposition which takes place in a resin and diachylon base

plaster, will at once agree as to the superior keeping qualities of an India rubber plaster. In the writer's practice he has known India rubber base plasters to keep perfectly for fifteen years.

The making of India rubber plasters is hardly within the province of a retail pharmacist. In fact, it is an art which requires the installation of large and expensive apparatus. The process has often been described. It is perhaps sufficient to state that the processes outlined in the United States Dispensatory are substantially correct.

Rubber plasters, for the most part, are made by combining India rubber, two parts, with burgundy pitch, one part, and to this is added gum, olibanum, galbanum, wax, sometimes olive oil, fillers, such as orris root, to complete the mass. Masses of this character vary with each individual plaster or medication, an acceptable plaster being one which shall contain at least 33 ⅓ per cent. rubber.

The rubber to be used in a plaster mass is crushed, washed in alkaline water to remove the natural acids, resins, dirt, etc., it is then ground until plastic, and combined with the gums and with the medicaments. The process of crushing, grinding, and mixing is conducted by means of large iron rollers, an essential feature of the process being the use of great pressure instead of the heat employed in the ordinary process of plaster making. The plasters are finally spread upon the cloth by means of heavy iron rollers, on an apparatus known as a calender. In the writer's laboratory this calender weighs 20,000 pounds, and here the spreading is accomplished by pressure and the avoidance of heat. The finished plaster after being spread is allowed to stand or set. It is then wound upon cylinders, cut into shapes and lengths, such as rolls of varying widths and lengths, or into the ordinary size, 5 x 7½ inches, the latter usually being perforated.

In the eighth revision of the Pharmacopœia a notable change was made in the formula for plasters by introducing a new mass under the title of "Emplastrum Adhæsivum" as follows:

EMPLASTRUM ADHÆSIVUM
Adhesive Plaster

Rubber, cut in small pieces, twenty grammes	20 Gm.
Petrolatum, twenty grammes	20 Gm.
Lead plaster, nine hundred and sixty grammes	960 Gm.
To make one thousand grammes	1000 Gm.

"Melt the rubber at a temperature not exceeding 150° C. (302° F.); add the petrolatum, and continue the heat until the rubber is dissolved. Add the lead plaster to the hot mixture; continue the heat until it becomes liquid, then strain, allow it to cool, and stir until it stiffens."

The mass here given was intended as an adhesive plaster, and also to be used as a base or vehicle for belladonna plasters, capsicum plasters, and opium plasters. In the previous edition of the Pharmacopœia the base or mass in most instances had been a combination of resin and lead plaster masses. Masses of this character had been official in several of the previous revisions. It has been stated that the present mass was introduced for the reason that non-rubber plasters had been entirely superseded by plasters with a rubber base, and that while non-rubber plasters had been retained in the U. S. Pharmacopœia in the several revisions, they had become entirely obsolete, and it was the intent of this innovation to improve the plaster mass so as to make them respond to the requirements for an India rubber base plaster.

It has been stated that the formula of the Pharmacopœia would enable the pharmacist to prepare and spread rubber base plasters, and that as a final result the lost art of plaster spreading would be restored to pharmacy. Experience, however, has shown that plaster spreading in pharmacy is no more popular to-day than when the present edition of the Pharmacopœia was issued, and, indeed, the present mass of the Pharmacopœia is not as popular as were the plaster masses of the previous Pharmacopœia.

The reasons for this condition are plain. The mass of the Pharmacopœia contains 2 per cent. of rubber, 2 per cent. of petrolatum, and 96 per cent. of lead plaster. This falls far short of the requirements for an India rubber plaster mass. The India rubber adhesive plasters, such as are sold in the market at the present time, contain from 20 to 50 per cent. of India rubber; the medicated India rubber plasters contain from 20 to 40 per cent., and it is the use of India rubber in these proportions that gives to India rubber plasters their peculiar consistency and properties.

It is my judgment that the finished plaster mass of the Pharmacopœia contains little or no rubber, as such. In making up the mass it is required that the rubber shall be melted at a temperature of 150° C. (302° F.), it is then combined with petrolatum and lead plaster mass. India rubber is decomposed at a temperature

below the point named. India rubber is decomposed in the presence of almost any fat, and especially in the presence of petrolatum. India rubber is rapidly decomposed under the influence of heat, it is also decomposed in the presence of many metals, and it is especially acted upon by lead. Such a combination, in the course of time, has a tendency to harden and become entirely useless as a plaster mass, and it would be better from a therapeutic and mechanical point of view if the India rubber had been omitted from the formula altogether. It is my judgment that the finished mass is not at all comparable with the diachylon mass, or the resin mass of the former Pharmacopœias.

The mass of the present Pharmacopœia, when freshly made and warm enough to spread, is a soft, sticky, unusable stuff. It is not to be wondered at that the profession have never adopted plasters made by the present Pharmacopœial methods, and that they rely as heretofore upon India rubber plasters, or the resin and lead plaster masses.

In addition to the plasters which I have named, the U. S. Pharmacopœia VIII has a formula for mercurial plaster made up with metallic mercury, the oleate of mercury, all combined with a lead plaster base. In this formula hydrous wool fat is used for the purpose of extinguishing the mercury. There are also given formulas for lead plaster and soap plaster, the latter being a combination of soap and a lead plaster base.

Diachylon plaster has a fairly good sale, but inquiry reveals the fact that the most of it is purchased ready spread under the types known as Maw's and De La Cour's. These types correspond quite nearly to the diachylon plaster of the U. S. Pharmacopœia of 1890, or the British Pharmacopœia of 1898, with the addition of a certain amount of resin.

The process given for capsicum plaster in the last revision directs that the oleoresin of capsicum be smeared over adhesive plaster. This process affords a convenient way of obtaining the effects of capsicum, and is capable of considerable amplification, and points out a method whereby medicated plasters may be prepared extemporaneously. Medicaments usable as external applications may be brushed over the surface of adhesive plaster and an infinite variety of medicated plasters prepared at short notice.

In this connection I call attention to the fact that, in addition

to the ordinary uses for India rubber adhesive plaster in operative surgery, there is a rapidly increasing field opening for its use as a therapeutic application. A glance at the medical journals of the last few years reveals many methods whereby such an application is being made. For example, I note the application of adhesive plaster in various forms for corns, bunions, swellings, inflammations, glandular enlargements, œdema, mammitis, mammary abscess, inflamed joints, gout, rheumatism, effusions, varicose veins, ulcers, pleurisy, pleuropneumonia, hiccough, bronchitis, neuralgia, lumbago, prolapsed stomach, floating kidney, excessive sweating, frost bites, tuberculosis, adenoids, boils, carbuncles. These varied and constantly increasing uses suggest that possibly in many instances medicated plasters would be indicated, thus giving the action of certain medicaments in addition to the mechanical and physical action of the plaster. One writer has suggested the covering of the part, to which adhesive plaster is applied, with certain medicinal agents and then applying the plaster. The process which I have outlined of brushing or spreading the medication over adhesive plaster would seem to be the more acceptable.

In the Pharmacopœia of 1880, belladonna plaster was prepared with the alcoholic extract of the root. This was also the case with the British Pharmacopœia of 1898. The revisions of the U. S. Pharmacopœia of 1890 and 1900, however, substituted the extract of the leaf for that of the root. No good reason seems to have been advanced for this change, and many reasons could be urged in favor of the extract of the root.

A plaster of the strength of that of the present Pharmacopœia, made with the extract of the leaf, is so filled with the peculiar waxy, resinous constituents of the leaf, and so colored with chlorophyll as to be highly objectionable. The belladonna plasters of the market are made almost entirely from the root. A plaster thus made either by using the base of the Pharmacopœia or an India rubber base, is easier to spread, more adhesive, and altogether more desirable than that made from the leaf, and in my judgment in the forthcoming revision the extract of the root should be restored to its former place in the making up of a plaster.

Neither the Pharmacopœia of 1880 nor that of 1890 established a definite alkaloidal strength for belladonna plaster. As a consequence belladonna plasters could be found in the market varying all the way from the slightest trace of alkaloid up to and above

the amount now prescribed as the standard. The result was not only confusing, but in certain instances serious consequences arose therefrom. The eighth revision of the Pharmacopœia established the standard of 0.38 to 0.42 per cent. alkaloid. The British Pharmacopœia of 1880 had no definite alkaloidal standard for this plaster, but the British Pharmacopœia of 1898 prescribed that belladonna plaster should contain 0.5 per cent. of the alkaloid of belladonna root.

It is the opinion of many authorities that both of these standards are high. Numerous instances have arisen whereby the constitutional effects of belladonna have been produced by the application of belladonna plasters. The Pharmaceutical Society of Great Britain has promulgated a formula for a milder belladonna plaster standardized to 0.25 per cent. alkaloid, giving as a reason therefor that a plaster of such a strength was less likely to produce poisonous symptoms than that made in accordance with the British Pharmacopœia.

My suggestion would be that the standard strength for belladonna plasters should be 0.3 per cent. of the alkaloids of belladonna.

In addition to the plasters of the Pharmacopœia, we find a number of kinds in the National Formulary. In the third edition of this book we have aromatic or spice plaster—a combination of cloves, cinnamon, ginger, capsicum, and camphor, with cottonseed oil and lead plaster as a base; camphorated brown plaster, which resembles the camphorated mother's plaster of the German Pharmacopœia, and is made up of red oxide of lead, olive oil, and camphor; compound tar plaster, which is composed of tar, podophyllum, and poke root combined with resin. These last two plasters are of the nature of the old time sticking salves, scarcely resembling the modern conception of a plaster.

In the addenda to the National Formulary we have ammoniac plaster, which is made up entirely of gum ammoniac; ammoniac and mercury plaster, consisting of gum ammoniac and oleate of mercury combined with a lead plaster base; arnica plaster, which is prepared with the extract of arnica root combined with resin plaster; asafetida plaster, a combination of asafetida, lead plaster, galbanum, and yellow wax; strengthening plaster, consisting of ferric hydroxide combined with olive oil, burgundy pitch, and lead plaster; burgundy pitch plaster, a combination of burgundy pitch, olive oil, and yellow wax; Canadian pitch plaster, consisting of

Canadian pitch and yellow wax; cantharidal pitch plaster, which is essentially the warming plaster of the U. S. Pharmacopœia of 1890 and is made up of cantharidal cerate combined with burgundy pitch; resin plaster, which is essentially the adhesive plaster of the U. S. Pharmacopœia of 1890, being a combination of lead plaster, resin, and yellow wax.

It should be noted that in the National Formulary there is no attempt to introduce India rubber into the compound, and that the formulas given in this work are those which have come down through the ages of pharmacy. It should also be noted that we have an adhesive plaster in the Pharmacopœia and an adhesive plaster in the National Formulary which are entirely different in their constituents, as well as in the resulting product.

In view of the fact that the National Pure Food and Drugs Law and the enactments of the various states have named the U. S. Pharmacopœia and the National Formulary as the standard for medicinal preparations, it seems imperative that the Pharmacopœia should name the standard for plasters in common use. Such being the case, and in consideration of the fact that plasters made with the official bases have but little or no sale, in my judgment, this course could be pursued with prescribing what the mass of the base or vehicle should be. In other words, latitude might be allowed in the selection of the ingredients of the plaster other than the medicament. This course would allow the plaster maker or the dispenser to supply plasters to suit the demand; it would enable the physician to know the exact amount of medication present in a given plaster mass, whatever might be the vehicle employed.

In my judgment the Pharmacopœia should also prescribe processes by which plasters, especially those containing alkaloids, could be assayed. The law and trade customs now require that there shall be some authority to which all things may be referred, and the Pharmacopœia alone is such an authority, and whatever else we find in such a work we should find the standard for medicinal preparations and the methods by which a given substance may be compared with the standard.

Rather than to eliminate from the Pharmacopœia a single plaster or a single preparation for which there is a reasonable demand, I would urge the addition of a still greater number. I have also suggested to the revisers of the Pharmacopœia that the formulas for plasters should be revised: That the mass or base introduced

into the last revision under the head of "Adhesive Plaster" should be abandoned, and a mass or base more nearly resembling that of the old base of 1880 be restored: That if such a course could be made possible, the alternate use of any India rubber mass, such as now employed by manufacturers, be allowed: That assay processes be prescribed for all plasters containing alkaloids or definite medicinal medicaments.

SCAMMONY AND RESIN SCAMMONY.*

By H. Engelhardt and M. R. Schmidt.

Considerable work has recently been done on the chemical and physical properties of the several substances generally classed as scammony resins. Guigues,[1] Cowie,[2] and Taylor[3] have made important contributions to our knowledge of these bodies, but it appears that the end is not yet reached.

The whole subject is more complicated than would appear at first sight, and great confusion exists, especially in the minds of dealers, as to what is covered by the terms scammony and resin scammony.

The U.S.P. recognizes as official two substances: scammony, which is the exudate obtained by incising the living root of *Convolvulus scammonia,* and resin scammony, which is prepared by extracting scammony with alcohol, precipitating the resin with water, and drying at a gentle heat.

The French Codex recognizes the same substances.

The British Pharmacopœia, on the other hand, describes virgin scammony, resin scammony, and scammony root; the virgin scammony is used without further purification, and the resin scammony is made by extracting scammony root with alcohol. Consequently resin scammony of the British Pharmacopœia is not necessarily identical with resin scammony of the U.S.P. or the French Codex.

Of late years there has appeared on the market another substance, the so-called Mexican scammony, prepared by extracting

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* Read at the meeting of the A. Ph. A. at Richmond, Va., May, 1910.

[1] *Journ. de Ph. et de Ch.* (6) 11; 529 (1900); *ibid.* (6) 22; 24 (1905); *ibid.* (6) 24; 404, 440, 498 (1905); *Bull. Soc. Chim.,* 872 (1908).

[2] Trans. Brit. Pharm. Conf., 1908; 457, 462; *Pharm. Journ.,* Dec. 25, 1909.

[3] Am. Journ. Pharm., vol. 81, 105 (1909).

the root of *Ipomœa orizabensis*. This substance is not yet official in any of the pharmacopœias.

The subject is further complicated by the difficulty of procuring authentic samples. The dealers frequently confuse names, and, judging by our analytical results, substitution very often takes place. As an example, one lot of root shipped as genuine Mexican scammony was labelled "Convolvulus Scammonia, Mexican," which is of course contradictory.

The work of Guigues dealt principally with the solubility of scammony resin in ether, and with the optical rotation. He found that some scammony resins were partly insoluble in ether, while the resin from *Ipomœa orizabensis* is completely soluble in ether and can be used to adulterate true scammony, a statement, which, as will be shown later, is incorrect. He also called attention to the necessity of using ether of a definite degree of hydration and alcohol percentage when determining the solubilities.

As regards the optical rotation for resin extracted from the gum resin (scammony), Guigues found a maximum specific rotation of —24.5°. For resin extracted from the root, the rotation varied from —18.5° to —23.5°.

The work of Cowie showed that the saponification value is a simple and accurate means of distinguishing true scammony resin from Mexican resin. Cowie also studied the solubility in ether.

Taylor has also made a rather extended study of the acid and saponification numbers, ether solubilities, and iodine numbers of various scammony resins. According to his statement, however, all these resins were prepared by extracting the roots with alcohol, and hence none of them can be regarded as U.S.P. products.

Cowie does not give any details as to the history of most of his resins, but it appears that most of them were commercial samples, or purified resins obtained from commercial articles. If his resins were prepared by purifying virgin scammony, they would come under the class of the U.S.P. resin scammony, but would not be official in the British Pharmacopœia, and vice versa, if they were made by extracting the drug, they would be official in the British Pharmacopœia and not in the U.S.P. This instance shows the difficulty of arriving at definite conclusions in these matters.

The chief results of Taylor's and Cowie's work have been to show that the saponification values for resins from *Convolvulus scammonia* range around the number 238, while the saponification values

of the resins obtained from the Mexican root are generally less than 190. Taylor, using U.S.P. ether, found that both the Mexican and the true scammony resins, with the exception of one sample, were at least 99 per cent. soluble in ether. This does not agree with the statement of Cowie, who finds that true scammony resin is soluble from 96.4 per cent. to 100 per cent. in ether of sp. gr. .720, while three samples of the Mexican resins were dissolved only to the extent of 68.6 per cent. to 72 per cent. Cowie has directed attention to the varying solubility which will be found if the ether used in the different determinations is not perfectly uniform in quality. This fact may account for the discrepancies between Taylor's and Cowie's results. A more detailed discussion of this point will be taken up later.

The resins examined in this work were all purified according to the U.S.P. method, *i.e.*, extracting with boiling alcohol, with precipitation of the concentrated extract by water and subsequent drying. In order to insure more perfect drying, without the danger of overheating, all our resins were dried in the following manner. After thorough washing, the resinous mass was freed from inclosed water by stirring and draining. It was then dissolved in alcohol, filtered, and the alcoholic solution evaporated to a thick syrup, which was then poured on thin sheets of glass and dried at a temperature slightly below 100°. The results show that the moisture content of resins dried in this way is no less than is found in those which have been dried by other methods. The alcohol was certainly eliminated, but it appears that a temperature above 100° is necessary to remove the water entirely. The U.S.P. direction to dry at "a gentle heat" therefore seems inadequate.[1]

The moisture determination was made by heating the powdered resin on a watch glass for one hour at 110° to 115°. Our results are practically identical with those of Cowie and Taylor, and the same is true of the percentage of ash.

The determination of the acid number often offers considerable difficulty, on account of the dark color which the solution assumes almost immediately after the addition of any alkali. Recourse was finally had to the method of Marx.[2] Two grammes of the powdered resin are dissolved in a large flat-bottomed porcelain dish in

[1] The French Codex directs 45° C.

[2] *Chem. Ztg.*, No. 16, 1910.

about 100 c.c. of neutral alcohol, and the titration made with one-half normal alcoholic potash and phenolphthalein. The solution of the resin is thus brought against a white background, in a thin layer, which facilitates the determination of the end point. Even with this aid, however, the determination is not always satisfactory, and little confidence can be placed in the accuracy of the results. An attempt to use $\frac{N}{4}$ barium hydrate solution was unsuccessful, since the color developed, if anything, was darker than that caused by the potassium hydroxide.

The saponification values were determined in the usual way, using $\frac{N}{2}$ caustic potash.

Ether solubilities were determined in both commercial and anhydrous ether. The commercial ether had a sp. gr. of .7128 at 25°, while the anhydrous ether had a sp. gr. of .7106. It will be noted, as Cowie has already pointed out, that the ether solubility varies with the nature of the ether used.

A rather extended study of the iodine numbers was made. The method by Hübl was applied at first, but it was found to be impossible to obtain concordant results by it. The iodine numbers varied in some cases 100 per cent. when the different tests were allowed to stand for different lengths of time. Moreover, no definite end-point could be found when titrating the excess of iodine with sodium thiosulphate and starch indicator. The solution continually became blue within ten seconds after being decolorized, and this often continued during the addition of 3 to 5 c.c. of thiosulphate solution. This method was finally given up and the determinations were made according to the method of Wijs.[1] This method has proven itself to be so satisfactory that we can recommend it most highly, at least when working with these resins. The solution is prepared as follows: 9 Gms. of powdered iodine are dissolved by the aid of heat in 500 c.c. of glacial acetic acid. Chlorine gas, washed through water, and dried by sulphuric acid, is then passed into the solution, using a capillary tube to insure more complete absorption. Thus the iodine is converted into iodine monochloride. The completion of the reaction is shown by the sudden disappearance of the dark-brown color of the solution, and this end-point is very

[1] *Berichte*, 31; 750 (1898); *Chem. Rev. Fett-u. Harz-Ind.* 6; 5; see also the excellent article by Harvey, *Journ. Soc. Chem. Ind.* 21; No. 23, 1437 (1902).

easily seen. About one-tenth of a gramme more of iodine is added, until the dark color of the solution is partly restored. This is done to prevent the solution containing an excess of chlorine. To make a determination, 1 Gm. of the powdered resin is put into a glass-stoppered 200 c.c. bottle, 10 c.c. of redistilled carbon tetrachloride free from carbon disulphide or oxidizable substances are added, and 25 c.c. of the iodine monochloride solution. After standing for one hour in the dark, 20 c.c. of 10 per cent. potassium iodide solution are added and 50 c.c. of distilled water, and the excess of iodine titrated back in the usual way. The end-point is very sharp and there is very little tendency for the blue color to reappear. One sample which was allowed to stand for 15 hours required only 0.3 c.c. more of tenth-normal thiosulphate solution to titrate the iodine which had separated.

The iodine numbers obtained by Wijs's method were in every case higher than those obtained by Hübl's method, even when the latter solutions were allowed to stand for twenty-four hours. Blank determinations are unnecessary with Wijs's method. The equivalent of 25 c.c. of the solution in terms of sodium thiosulphate solution is determined once for all, and the solution is so stable that subsequent blanks are not necessary. The solution of iodine monochloride can be prepared in one-half hour, and for most oils and fats from fifteen to forty minutes is sufficient time for complete absorption of the iodine. The behavior of the scammony resins toward Hübl's solution led us to consider one hour as a sufficient time, but it may be said that no difference was found when the absorption was continued for one-half hour longer.

The optical rotations were determined with the decolorized resin in the following way: about 4 Gm. of the resin were dissolved in about 50 c.c. of alcohol, water added almost to turbidity, and the solution boiled for one hour with about 2 Gm. of animal charcoal, using a reflux condenser. After settling, the solution is cooled, and the liquid poured through a filter. A second treatment with animal charcoal generally suffices to give a solution which is almost colorless. After filtering, 10 c.c. of this solution are removed by a pipette to a small tared beaker, evaporated to dryness, dried at 110° and weighed. Another portion of the solution is polarized in a 10 cm. tube.

In order to confirm the results of previous observers, and to orient ourselves regarding virgin scammony and Mexican scammony

resin, the specimens marked I, II, III, and IV in the tables were prepared. Number I came to us labelled "Virgin Scammony, elect." In its physical appearance it agreed with the descriptions in the text-books. It was of a greenish-brown color, very brittle, and its lustre would have been classed as subresinous in mineralogy, since the fracture was almost without gloss. It was also of a granular or porous texture. No gross impurities were visible, such as pebbles, woody matter, etc. In our opinion, this sample was actually the exudate from *Convolvulus scammonia,* which had possibly been freed from coarse impurities by fusing and straining.

A purified resin obtained by extracting a portion of I with alcohol, precipitating with water, etc., constitutes specimen II. Number II presented an appearance entirely different from I. It was of a yellowish-brown color, semitransparent, not very odorous, and its lustre was markedly resinous.

III was prepared by percolating a lot of root which had been labelled "True Scammony Root." Microscopic examinations bore out this statement.

IV was obtained by percolating a lot of drug identified as *Ipomœa orizabensis.*

These samples were compared with three products marketed under the names of virgin scammony and scammony resins. Specimen V was labelled "Scammony Resin Virgin." Its appearance was totally different from that of I, its lustre was perfectly resinous, its color dark brown, and instead of being porous, the pieces were perfectly homogeneous like ordinary resin. Its odor, moreover, was cheese-like. Judging from its appearance, and more especially from its physical and chemical constants, this sample was wrongly labelled. Before use it was purified in the usual way.

Specimen VI was labelled "True Scammony Resin," and in general appearance was identical with V. This sample had also been misbranded.

Sample VII was labelled "Resin Scammony." In appearance it was like V and VI, but its odor was slightly like pepper. It was examined both in the ordinary state in which it was received, and after having been purified, the purified sample constituting specimen VIII. The results show that it was also made from the Mexican root, and therefore was wrongly labelled.

The following results were obtained and are arranged in three tables. Table I includes moisture, ash, acid, saponification and ester

numbers. As stated before, the moisture content of these resins was not reduced by the method of drying adopted by us. The results agree perfectly with those found by Cowie and Taylor and no further comment is necessary, except to call attention to the high percentage of moisture in the commercial samples I and VII.

The percentage of ash is rather constant, and in all cases except I is well below the limit of 1 per cent. allowed by the U.S.P. for resin scammony. The percentage of ash found in I is also below the limit of 3 per cent. allowed by the U.S.P. for virgin scammony; this high percentage of ash confirms our belief that the resin had been only superficially purified by straining from gross impurities.

Nothing definite can be concluded from the acid numbers, as has already been stated by Taylor and Cowie. The saponification numbers, on the other hand, fall into two well-defined groups. I, II, III have saponification numbers which are considerably over 200. II, which may be taken as a representative sample of purified virgin scammony, has the value 236.6 which is in close agreement with the average of about 238 found by Taylor, Cowie, and others. The saponification value of the other five samples range within narrow limits around the number 177, which is lower than the average saponification value obtained by Taylor and Cowie.

Table II shows the solubility in various solvents. The most important results are the solubility in ether. Cowie and Guigues have, as already stated, directed attention to the necessity of using anhydrous ether in determining the solubility, and their results are fully confirmed by the present work.

Sample I, the most impure specimen of all, was soluble to the extent of 71.8 per cent. in dry ether, but to the extent of 85 per cent. in commercial ether, thus passing the requirements.

Sample II, the purified resin prepared from I, was entirely soluble both in anhydrous and commercial ether. III was soluble to the extent of 96 per cent. in commercial ether, and by stretching the words "almost completely" might have passed muster as the U.S.P. article, although it was prepared by percolating scammony root. The other five specimens vary between 80 and 90 per cent. soluble in hydrous ether, and were all nearly 90 per cent. soluble in anhydrous ether. In this connection we must call attention to the phenomenon always noticed when dissolving Mexican scammony in ether. Using U.S.P. ether, containing varying amounts of water and alcohol, a part of the resin invariably separates

as a varnish on the walls of the vessel. This does not take place with resin made from scammony or from scammony root, and this appearance can be used to detect Mexican scammony in the presence of a considerable quantity of true scammony resin. Using anhydrous ether, the insoluble portion assumes a granular form, which on standing settles to the bottom as a sticky mass.

The portion insoluble in chloroform was generally gelatinous and rather dark in color.

We have already spoken of the difficulty encountered in determining the iodine numbers by the method of Hübl. For example, sample II after being allowed to stand for four hours gave an iodine number of 5.5; after standing for fifteen hours this value had risen to 8.8; and another test which was allowed to stand for twenty-four hours showed only 8.22. Sample V with Hübl's method gave 8.38 after five hours and 10.58 after fifteen hours, while the same resin by Wijs's method gave 11.6 in one hour. The average of our iodine values is slightly greater than the average of Taylor's. As can be seen from the tables, no definite relation exists between the variety of resin and the iodine value, and this method cannot be used as a means of differentiating the resins. We wish, again, however, strongly to recommend the method of Wijs. It is convenient, rapid, and accurate, duplicate determinations agree well, the end-point is sharp, and work is considerably lessened by the fact that the solution is stable and blanks are unnecessary for each determination. The solution should be kept in a dark bottle, otherwise the acetic acid is likely to be substituted by the halogens and the solution will lose in strength.

The specific rotations also fall into two distinct groups. The values found for the resins known to be derived from *Convolvulus scammonia* are close to —24°, while those for the Mexican resins are all over —31°. Guigues, as mentioned before, was the first to call attention to this fact. Our value of —25.98° for sample I is slightly higher than his maximum of —24.5° obtained for a specimen prepared in an identical manner, and our value of —24.24° for sample III is slightly higher than his limit of —23.5° for resin extracted from the true root. These determinations can be made with a considerable degree of accuracy, and the optical rotations furnish a valuable means of distinguishing the true and false resins. The specific rotation of the Mexican resin approaches the specific rotation of resin jalap, but the high price of resin jalap would prevent any adulteration of Mexican resin with the former.

It is a well-known fact that virgin scammony is getting to be a scarce article, and it is almost impossible at the present time to obtain any large quantities of the authentic substance. Moreover, all the work that has been done so far goes to show that the resin prepared by extracting the root of *Convolvulus scammonia* is practically identical with resin scammony prepared according to the U.S.P. directions from virgin scammony. We would suggest, therefore, if resin scammony is to be retained in the Pharmacopœia, that the Revision Committee make the resin extracted from the root official, as has been done in the British, Belgian and Italian Pharmacopœias. On the other hand, if it can be shown by physiological experiments that the Mexican resin is identical in its action with true resin scammony, there seems to be no good reason why that cheap and abundant article should not replace the latter.

TABLE I.

Sample.	Moisture. Per Ct.	Ash. Per Ct.	Acid No.	Sap. No.	Ester No.
I.	6.16	2.70	18.5	207.2	188.7
II.	1.95	.00	10.6	236.6	226.0
III.	2.07	.21	16.3	256.2	239.9
IV.	1.45	.20	10.2	175.8	165.6
V.	2.25	.07	12.2	177.1	164.9
VI.	2.23	.20	14.0	171.6	157.6
VII.	4.29	.30	13.6	183.8	170.2
VIII.	2.03	.15	14.9	175.9	161.0

TABLE II.

Sample.	Soluble in Abs. Ether.	Sol. in U.S.P. Ether.	Sol. in Chloroform.	Sol. in Alcohol.
	Per Cent.	Per Cent.	Per Cent.	Per Cent.
I.	71.8	85	82.1	90.6
II.	100	100	100	100
III.	93.9	96.0	100	100
IV.	89.4	84.1	98.0	100
V.	90.2	85.5	98.9	100
VI.	88.3	80.9	96.1	100
VII.	89.6	82.0	96.9	100
VIII.	90.4	91.5	97.4	100

TABLE III.

Sample.	Iodine No.	Optical Rotation. Degrees.
I.	11.69	—25.98
II.	10.45	—24.97
III.	17.83	—24.24
IV.	11.60	—32.78
V.	11.48	—33.80
VI.	13.93	—34.27
VII.	12.46	—31.31
VIII.	11.65	—31.83

LABORATORIES OF SHARP & DOHME,
Baltimore, Md.

A NOTE ON OIL OF GAULTHERIA.*

BY GEORGE M. BERINGER.

Early in June of last year, I had collected near Hammonton, N. J., a quantity of the plant *Gaultheria procumbens L.* and expressed to me in the fresh condition. This was carefully garbled over to remove any admixed plants or leaves, and adhering dirt washed off. It was then distilled in a copper still with jet of live steam continuously thrown into the still, so as to prevent charring and at the same time thoroughly extract the oil. From 4070 Gm. of the plant I obtained 23.63 Gm. of oil, equivalent to a yield of 0.586 per cent. It is to be noted that the writer used the entire plant for his experiment.

About the same time, Professor Henry Kraemer had distilled in his laboratory at the Philadelphia College of Pharmacy a quantity of gaultheria, using the leaves only which were separated from the freshly collected plants. The writer was fortunate enough to secure a sample of this oil and so has now two authentic samples of oil of gaultheria to exhibit.

While it is true that the U. S. Pharmacopœia does describe oil of gaultheria as "distilled from the leaves," it is exceedingly doubtful if in actual practice this has ever been strictly followed as

* Presented to the New Jersey Pharmaceutical Association meeting, Cape May, June 15, 1910.

the custom is to gather over ground portions of such small procumbent plants and not expend the labor necessary to strip leaves only.

These two samples of oil exhibit some distinct differences. The sample from Kraemer's distillation is almost water white and has remained so for a year. It has a much lighter, more ethereal odor while that from my own experiment has gradually darkened and assumed a pale amber tint and has a much heavier odor: both color and odor more closely resembling that of the distilled oil commonly appearing in commerce.

The specific gravity and optical rotation of these oils is as follows:

	Sp. Gr.	Optical Rotation.
Kraemer's	1.1785	—0.26°
Beringer's	1.177	—1.335°

While there is scarcely any difference in the specific gravity of the samples there is marked difference in the lævo-rotatory power. In this connection the U. S. Pharmacopœia states that oil of gaultheria is lævo-gyrate up to —1° in a 100 mm. tube, at 25° C. If the oil from the entire plant is to be officially recognized then the writer's experiment demonstrates that this limitation must be somewhat extended.

PROGRESS IN PHARMACY.

By M. I. Wilbert, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

The meetings of state and national associations, both medical as well as pharmaceutical, that have been held during the past three months are destined to have a very far-reaching influence on the future development of pharmacy.

The proceedings of the several state pharmaceutical associations have been reported at length in the several trade journals and from the published reports it would appear that the meetings were unusually well attended and that considerable time was devoted to the discussion of scientific papers and subjects.

As usual the proceedings of the Missouri Pharmaceutical Asso-

ciation are the first to be published, and Secretary Whelpley is to be congratulated, not alone for his promptness, but also for presenting so complete a report in the short time intervening. The book contains 177 pages and is liberally illustrated. The meeting of the Missouri Association was held in Maryville, June 14–17, 1910, and was quite an innovation in that the members occupied a tent city.

THE MEETING OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION will no doubt serve to arouse interest, not alone in Pennsylvania, but throughout the several states of the Union. A comprehensive legislative program was outlined and put in effect the resulting laws will establish for American pharmacy a new and decidedly higher ideal than has been evidenced heretofore.

In the matter of scientific papers the Pennsylvania Association again leads all of its competitors and the association honored itself by electing to the presidency Prof. Chas. H. LaWall who, for a number of years, has been directly responsible for the unusually large number of papers read at the meetings of the Pennsylvania Pharmaceutical Association.

THE AMERICAN CHEMICAL SOCIETY.—The summer meeting of this society was held in the city of San Francisco, July 12–15, 1910, and while not so largely attended as some of the previous meetings in the eastern section of the United States, appears to have been thoroughly satisfactory to the members who had an opportunity to attend.

AMERICAN MEDICAL ASSOCIATION.—The sixty-first annual meeting of this association was held in the city of St. Louis, June 6–10, 1910. From published reports it would appear that from a scientific or an organization point of view the meeting was a complete success.

The attendance was a little over four thousand, a number exceeded only by the meeting in Chicago, in 1908, and Boston, in 1906. Every section is reported as having held profitable sessions and the attendance at the section meetings is said to have been unusually good.

THE SESSIONS OF THE SECTION ON PHARMACOLOGY AND THERAPEUTICS were unusually interesting to pharmacists and many of the local men took advantage of the opportunity to attend and take part in the discussions.

The pharmacists of St. Louis also made a practical contribution to U.S.P. and N.F. propaganda work by exhibiting a number of

official preparations. This exhibit, and a somewhat similar exhibition from the chemical laboratory of the American Medical Association, elicited considerable attention and both were favorably commented on by the physicians who saw them.

BRITISH PHARMACEUTICAL CONFERENCE.—The forty-seventh annual meeting of the British Pharmaceutical Conference was held in the town of Cambridge during the week of July 25, 1910. The meeting has been designated as one of the best of recent years and from the published reports it would appear that it brings with it very marked changes in the association work of British pharmacists. The presidential address by Mr. Francis Ransom is a contribution of unusual merit and well worthy of careful study by American pharmacists.

The papers, according to the established custom, are reported at length in the pharmaceutical journals and while not numerous they indicate careful study and are fully representative of the scientific attainments of British pharmacists.

The paper on Liquid Extract of Ergot, by J. H. Franklin, with results of physiological tests made by G. S. Haynes, is a particularly timely one and indicative of the tremendous field for research and study that is available to pharmacists at the present time.

Several papers were devoted to the bacteriological testing of disinfectants, the object being to evolve, if possible, a method for the standardization of disinfectants. The president, in his address, points out that the difficulties met with in the investigation appear to be as great, and even greater, than those encountered in the standardization of drugs. Neither the chemical nor the bacteriological processes which hitherto have been devised seem to be applicable in all cases, although for specific purposes comparisons of efficiency may be deduced.

The social features of the meeting were, as usual, quite numerous, and the week's gatherings are generally considered to have been a complete success. The next annual meeting will be at Portsmouth and the president elected to preside at that meeting is W. F. Wells, of Dublin.

FEDERATION OF LOCAL PHARMACEUTICAL ASSOCIATIONS OF GREAT BRITAIN.—A news note points out that at the meeting of this association, held in Cambridge, on Tuesday, July 26, it was resolved to recommend that the British Pharmaceutical Conference

divide its proceedings into scientific and practical sections, the latter, including some of the matters which the conference has been in the habit of dealing with, would suffice to include the work now being done by the Federation of Local Pharmaceutical Associations of Great Britain, and the latter organization, which was founded to represent the trade interests of British chemists and druggists, is to be discontinued (*Chem. and Drug.*, London, July 30, 1910, p. 154).

BRITISH MEDICAL ASSOCIATION.—The annual meeting of the British Medical Association was held in London, beginning on July 22. One of the more interesting discussions was on the question of censorship of advertisements offered for insertion in the *British Medical Journal*. It was finally decided that this question should be carefully considered by the Central Council and that a report be prepared and submitted to the next representative meeting.

The exhibition, which is described at some length in the *Chemist and Druggist* (June 30, 1910, pp. 155–158), was particularly interesting from an American point of view, in that a very large number of preparations that have been eliminated from similar exhibitions in this country were shown.

SOCIÉTÉ DE PHARMACIE D'ANVERS has recently celebrated its seventy-fifth anniversary and the journal of the society, for June 15, 1910, is devoted to an account of the several features of the celebration and incidentally gives a review of the history and achievements of the society since its organization on May 29, 1835. The report is liberally illustrated with portraits of present and former officials and is supplemented by an appendix containing messages of greeting and felicitation from other pharmaceutical associations.

THE CENTENARY OF THE "JOURNAL DE PHARMACIE ET DE CHÉMIE, PARIS."—A comprehensive history of this journal from 1809 to 1909 has been published separately, making a volume of 102 pages, liberally illustrated.

The biographical sketches and portraits of past editors include such well known personages as: Parmentier, Boullay, Pelletier, Bouillon-Lagrange, Soubeiran, Planchon, and Riche, names well known wherever the science and art of pharmacy or chemistry are known or practised.

INTERNATIONAL CONGRESS OF PHARMACY.—The *Chemist and Druggist* (May 21, 1910, v. 76, pp. 91, 92) presents a report of

interviews with M. Derneville and M. Schamelhout, regarding the International Congress of Pharmacy to be held in the City of Brussels, September 1 to 4. The meetings are to be held in the Palais des Académies, one of the finest buildings of its kind in Brussels, and the proceedings will partake of a scientific as well as of a professional character. One of the more important questions that will be discussed will be the introduction of international methods of analysis and the use of uniform reagents. Trade interests will also be discussed at length, particularly the sale of specialties in the different countries and the formation of an international federation of pharmacists' associations.

THE REVISION OF THE U.S.P.—Never before has the Pharmacopœia of the United States attracted the attention of the more progressive members of the medical profession to the extent that is now evident, and it would appear to be desirable that members of the U.S.P. Committee of Revision and pharmacists generally acquire more than a superficial knowledge of the interest that is being evidenced and the thoughts that are being voiced. Many of the more progressive medical men appear to agree with Dr. Abraham Flexner who, in the Report on Medical Education in the United States and Canada (Carnegie Foundation for the Advancement of Teaching, Bulletin No. 4, p. 63), characterizes the pharmacopœia as "the traditional encyclopedic expression of the credulity of empiricism in medicine."

PHARMACOPŒIA REVISION.—W. A. Bastedo is quoted (*J. Am. M. Ass.*, 1910, v. 55, p. 166) as pointing out that while a large comprehensive pharmacopœia is not of necessity a disadvantage and, by allowing for a diversity of opinion, may be an advantage, medical teaching must be in advance of the profession and the selection of drugs for this purpose should be based on reliable pharmacologic and clinical data, regardless of the extent of their use.

THERAPEUTICS AS IT APPEARS FROM THE PRESCRIPTION FILE.—Dr. Julius Noer asserts that an examination of many thousands of prescriptions from the files in drug stores shows prescriptions by physicians of an inordinate mass of pseudotherapeutic agents. He believes that talismanic therapeutics did not die with Paracelsus, nor has the mother church in Boston a monopoly as a promoter of pseudoscience; and that the excellent work of the Council on Pharmacy and Chemistry of the American Medical Association is

not without cause and justification (*J. Am. M. Ass.*, 1910, v. 55, p. 343).

PHARMACOPŒIAL REVISION.—Dr. A. S. Loevenhart, in discussing the above, points out that the situation is not encouraging. The whole drug business is in a bad state in many ways. With some striking exceptions, the vast majority of drug houses are interested purely and simply in the making of money and are unconcerned with the question of public health. Moreover, our expectations with regard to the pharmacopœial convention have been absolutely disappointed. The convention was dominated by poor medical schools and the pharmaceutical associations in the interests of the drug trade. The convention refused to pass a resolution excluding from the Pharmacopœia drugs which are known to possess no therapeutic effect. It is impossible to use the Pharmacopœia with our students.

MEDICAL EDUCATION.—The Carnegie Foundation report on medical education has been widely commented on in medical and lay journals. While this report contains many statements of detail which may be criticised, the general trend of the report has been generally commended, particularly in lay journals which, like the New York Globe, argue: "If the doors of the state university, rich in educational opportunities, qualified to turn out real doctors, lawyers, engineers, and the like are open to all, why should the manufacture of feebly qualified professional men by others be tolerated at all."

NATIONAL FORMULARY AND THE AMERICAN MEDICAL ASSOCIATION.—Considerable space has been devoted, in recent issues of pharmaceutical and drug journals, to the discussion of the attitude taken by the American Medical Association Committee on National Formulary and the refusal to co-operate with the Committee on National Formulary in the revision of that book. Much of the published discussion is designed to confuse rather than correct existing opinions regarding the aims and the objects involved.

To be entirely clear in the matter it should be remembered that the American Medical Association through its Council on Pharmacy and Chemistry has adopted certain standards to which materia medica products are expected to comply, and it would be manifestly unfair for this association to require compliance with its standards by the preparations enumerated in New and

Non-official Remedies and endorse remedies contained in the National Formulary which obviously do not comply with either the letter or the spirit of the rules under which the Council is working.

The American Pharmaceutical Association, on the other hand, through its Committee on the National Formulary, has undertaken to supply a legitimate demand for authoritative and pharmaceutically reliable formulas for preparations that may or may not have therapeutic value.

The primary and, in a way, the sole object of these formulas is to secure uniformity so that a physician who chooses to use a National Formulary preparation, and writes for it as such, is assured of securing, from reliable pharmacists, preparations that are identical in strength and composition no matter where or by whom they are made.

It will readily be seen that while the objects in view in both instances are commendable they do not necessarily have much in common.

The American Medical Association, through its Council on Pharmacy and Chemistry, is endeavoring to educate physicians to the future use of acceptedly reliable medicaments, while the American Pharmaceutical Association, through its Committee on National Formulary, is attempting to supply pharmaceutically correct formulas for preparations that are, by many of the leading medical practitioners, no longer accepted as being in harmony with modern theories or practice.

As further illustrating the interest that is being manifested in rational therapy it would be desirable to call attention to a number of additional articles that have been published in medical journals. This would, however, be space consuming and for the present it may suffice to call attention to the following:

PHARMACOLOGIC FETISHISM.—Under this heading Wilfred M. Barton discusses a dozen pharmacologic questions which he designates as delusions, basing his arguments on what appears to him firm ground.

Among others, he points out the futility of using lead and opium wash in sprains, giving sparteine as a cardiac tonic and substitute for digitalis, using calomel as a cholagogue, ergot as an internal hemostatic, and sweet spirits of nitre as a diuretic or diaphoretic (J. Am. M. Ass., 1910, v. 55, pp. 284–287).

C. N. Branin, in commenting on the paper by Dr. Barton, points out that every drug mentioned by the latter has been largely used by physicians with real or fancied results. He suggests that there should be no tearing down without building up and it would be well, therefore, if iconoclasts would, at the same time that they are criticising old time remedies, suggest effective substitutes (*J. Am. M. Ass.*, 1910, v. 55, p. 520).

PH. GERM. V. AND POST-GRADUATE INSTRUCTION.—A news item points out that the tests in the forthcoming new edition of the German Pharmacopœia are so novel that the Prussian Government has instituted courses for instructing the inspectors of pharmacies in the new analytical methods.

It is also proposed to institute special post-graduate courses at various universities for the benefit of owners as well as of pharmaceutical assistants. It is pointed out that the rapid strides made during the past year in analytical chemistry render it practically necessary for the pharmacist to receive proper tuition in this respect to enable him to apply the knowledge thus acquired to the best advantage in his own interests (*Chem. and Drug.*, London, July 30, 1910, p. 137).

NOMENCLATURE.—G. Grossmann, in discussing the nomenclature of the German Pharmacopœia, points out that despite the fact that this book has been repeatedly revised it still contains a very large number of incomplete and misleading names. He asserts that the book should above all be practical and designed to facilitate the everyday work of the apothecary and, above all, it should be in harmony with the usages of the time for which it is intended. Many of the points that he calls attention to are equally applicable to our own U.S.P. (*Ber. d. Deut. Pharm. Gesellsch.* Berlin, 1910, v. 20, pp. 266–277).

SYNTHETIC REMEDIES AS OFFICIAL SUBSTANCES is the heading for a timely editorial in the *Pharmaceutical Journal* (London, 1910, v. 30, p. 753). In the pharmacopœias of all countries the nomenclature of synthetic remedies has proven to be a stumbling block for one reason or another. In most cases the systematic names are out of the question while the name that has been given them by the manufacturer, even in the countries where they can be used, are so well known to the laity that their use is a doubtful advantage. In addition to antipyrin, phenacetine, salol, and sulphonal, which have been included in all of the newer pharmacopœias, the

following have been found to occur most frequently: Airol, 2; aristol, 5; aspirin, 8; benzonaphthol, 4; betol, 2; creosotal, 4; dermatol, 14; dionin, 4; diuretin, 13; doutal, 14; β-eucaine, 4; euquinine, 3; heroin, 6; iodol, 4; lactophenin, 3; novocaine, 2; protargol, 6; pyramidon, 3; salipyrin, 11; salophen, 4; stovaine, 2; tannalbin, 6; tannigen, 4; tannoform, 3; trional, 13; urotropin, 7; veronal, 4; xeroform, 3. These popular or trade names are, however, but seldom included as the official title.

BRITISH PHARMACOPŒIA.—The British Pharmacopœia Committee of Reference in Pharmacy has presented a second report to the General Medical Council which is summarized in the *Chemist and Druggist*, for July 2, 1910, p. 52, and embodies the results of the work accomplished in connection with the revision of the British Pharmacopœia from November 18, 1908, to December 16, 1909. The report has been published complete by Messrs. Spottiswoode & Co., Ltd., 5 New Street Square, London, and may be obtained from them post-free for 1s. 1d.

SAFEGUARDING THE PUBLIC HEALTH.—So much has been said recently in connection with the possible extension of public health work that many druggists appear to be decidedly confused regarding the desirability of having work of this kind done under the auspices of the National Government. Much of this confusion is, no doubt, due to the positive misstatements that have appeared in some of the more widely circulated trade journals and it may be reassuring to at least some to learn that the so-called medical trust is not responsible for the origin of all public health legislation.

An editorial (*American Medicine*, 1910, v. 16, pp. 339–342), in discussing the general subject, points out that: "Opposition to a national department of health from any one who does not have some selfish interest liable to be restricted or regulated by the proposed plans is quite incomprehensible.

"The fallacious argument promulgated by the 'National League for Medical Freedom' against the proposed national department of health is not apt to deceive for long any but those who wish to be deceived.

"The people will soon realize the truth, that the forces behind the 'League for Medical Freedom' are not as lily white and free from ulterior motives as those exploiting it would like to convey. Unquestionably many have been attracted to this organization in good faith and with no other object than to further the principle

of medical freedom. When such people realize that the great bulk of the regular medical profession are heart and soul with the broadest possible freedom of medical thought, teaching, and practice, and awaken to the unselfish, self-sacrificing work of the men who are bending every energy to what seems to them the *summum bonum* of present day living—the prevention of disease, it is entirely probable that any reason for the 'League for Medical Freedom' will cease to exist."

The rational discussion of matters relating to the safeguarding of the public health and the prevention of diseases has been altogether too much neglected by pharmacists and it is gratifying, therefore, to learn that Prof. Joseph P. Remington discussed "The rôle of pharmacy in preventive medicine," at one of the sessions of the Section on Preventive Medicine and Public Health of the American Medical Association (*J. Am. M. Ass.*, 1910, v. 55, p. 557).

Prof. Remington very properly asserts that: "The words preventive medicine have to a commercial druggist, a significance which he has yet failed to grasp. . . ."

It is unfortunate, however, that much of the discussion following is from a point of view that is practically negligible at the present time. It would be difficult indeed to demonstrate that disease can be communicated by means of the prescription container, even granting that the average druggist took absolutely no precautionary measures in the way of cleansing or destroying such containers.

While it may be true that some few retail druggists are careless and not too cleanly, the fault for this shortcoming is to be placed primarily at the door of the pharmaceutical schools which have as yet failed to give adequate instruction in the value of cleanliness and hygiene in general.

THE INTERNATIONAL ENCYCLOPÆDIA OF ETHICAL NON-OFFICIAL PHARMACEUTICALS.—An editorial in the *Journal of the American Medical Association* (Aug. 6, 1910, p. 519) calls attention to an evident attempt to develop the commercial possibilities of a book along the lines of New and Non-official Remedies, published by the Council on Pharmacy and Chemistry. As an illustration of present-day enterprise the article is well worth reading, though the evidence, as presented, is not creditable to the physicians and pharmacists involved.

PHARMACEUTICAL MANUFACTURERS AND THE GREAT AMERICAN FRAUD.—Medical practitioners are beginning to take a greater in-

terest in the source of their medicaments and are taking cognizance of the part taken by pharmaceutical manufacturers in supplying all customers regardless of the use to which their products may be put.

An editorial in the *Journal of the American Medical Association* (July 2, 1910, v. 55, p. 34) in discussing the part taken by many of the larger manufacturers in supplying ready to market products to defraud the sick says: "Legally they may be within their rights but ethically and morally their course is iniquitous, and no amount of argumentative sophistry will justify the attitude of the manufacturing pharmacists who are willing to sell their products to any who will pay for them, no matter to what use the drugs are to be put."

Additional comments will be found in the same *Journal,* v. 55, pp. 40, 418, 613.

SOOTHING SYRUPS AND RETAIL DRUGGISTS.—A decidedly progressive step is evidenced by the resolutions recently adopted by the Philadelphia Association of Retail Druggists, condemning so-called soothing syrups containing morphine and cocaine and refusing to sell them. This action has been commented upon quite widely and it is to be hoped that the association will be successful in its efforts to induce the state legislature, at its next session, to eliminate from statute books the present law which permits the sale of these drugs, providing the objectionable ingredients are announced on the labels (*J. Am. M. Ass.,* 1910, v. 55, p. 607).

EHRLICH-HATA "606," is one of the many designations that have been employed for the substance that is creating unusual attention as a possible specific for a number of diseases that are known to be due to spirochetes. The new remedy promises to be the most valuable discovery in the field of materia medica since the introduction of diphtheria antitoxin. The substance, which chemically is said to be dioxydiaminoarsenobenzol ($C_{12}H_{12}O_2N_2As_2$), has been selected from a long list of substances that have been experimented with because of their supposed or actual destructive influence on spirochetes, a class of organisms that have been shown to be the causative factors in a number of transmissible diseases. The reported results obtained are all but marvellous and the lay as well as medical journals of Europe are filled with discussions of the possible curative value of the compound.

Ehrlich himself has wisely safeguarded the use of the sub-

stance and is unwilling to allow its commercial exploitation until satisfied that the remedy will prove to be comparatively safe in the hands of the general practitioner. In view of the fact that it is a compound more or less closely allied to arsenilic acid, which in its various forms has been the cause of many cases of blindness, the precaution appears to be exceptionally commendable (*J. Am. M. Ass.*, 1910, v. 55, p. 601, 609, 610).

ALCOHOL A DANGEROUS AND UNNECESSARY MEDICINE.—A book review calls attention to a book with the above title recently published by Mrs. Martha M. Allen, Superintendent of the Department of Medical Temperance for the National Woman's Christian Temperance Union. The book comprises a collection of expressions of opinion by medical writers and is well worth more than casual notice on the part of pharmacists who are anxious to free their calling from the widely made imputation that they are in effect liquor distributors (*J. Am. M. Ass.*, 1910, v. 55, p. 523).

ALCOHOLIC BEVERAGES.—The London correspondent asserts that: "The tendency of recent years has been to limit considerably the field of the utility of alcohol, and the amount consumed in the hospitals is a mere fraction of that consumed a few years ago." A recently issued manifesto signed by 101 physicians in North Wales appeals to medical men to join them in an endeavor to discountenance the popular error that alcoholic drinks are necessary for the promotion of health by refraining from their employment in the treatment of disease (*J. Am. M. Ass.*, 1910, v. 54, p. 2130).

OFFICIAL RECOGNITION OF ALCOHOLIC BEVERAGES is well shown by the following:

TABLE SHOWING THE RECOGNITION ACCORDED TO WINE AND DISTILLED LIQUORS IN THE SEVERAL NATIONAL PHARMACOPŒIAS.

	British	German	French	Swiss	Dutch	Austrian	Belgian	Hungarian	Japanese	Spanish	Swedish	Italian	Danish	United States
Brandy	+	+	o	+	o	+	o	o	o	o	o	+	o	+
Rum.....	o	o	o	+	o	o	o	o	o	o	o	o	o	o
Whisky	o	o	o	o	o	o	o	o	o	o	o	o	o	+
Wine.....	+	+*	?	+	+	+	+*	+	+*	+*	+	+	?	+

Pharmacopœias marked + ? contain only a general article on medicinal wines, but no tests for or descriptions of wine itself.

Pharmacopœias marked * contain a general descriptive article on wine but no standards for any particular kind of wine.

ANTIPYRIN.—G. O. H. Wallace (Lancet) records a case of acute poisoning by 10 grains of antipyrin. Within fifteen minutes of taking the drug the patient complained of faintness and suffocation and the face became "blotchy" and swollen. While being examined she suddenly collapsed and became unconscious, but revived, and after treatment in bed for two days recovered. The most marked features of the case were the rapid onset and recovery, a low temperature, and great prostration (*Pharm. J. Lond.*, 1910, v. 85, p. 130).

ANTITYPHOID VACCINATION.—Frederick M. Hartsock, Major, Medical Corps, U. S. Army, reports the results of 1100 inoculations or antityphoid vaccinations by means of the injection of dead typhoid bacilli. This, he asserts, is destined to be a practical measure of prophylaxis and will be particularly useful in the handling of typhoid epidemics. In his experience no untoward results were noted; all patients recovered promptly. Even in the limited number of cases (10) in which the reaction was severe the patients were able to attend to duty after 24 hours (*J. Am. M. Ass.*, 1910, v. 54, p. 2123).

BISMUTH MILKS.—Dr. Judson A. Hulse warns against the use of bismuth preparations in the shape of creams, milks, etc.

In a series of observations covering their administration to 21 infants suffering from acute gastro-enteric conditions, he failed to observe a sedative or astringent action in a single case. In a number of cases the bismuth milk passed through the entire alimentary tract practically unchanged, while in control observations it was found that the administration of bismuth subnitrate resulted in darkened stools, lessened amount of blood, and almost complete disappearance of mucus within the first twenty-four hours of its administration (*J. Am. M. Ass.*, 1910, v. 55, p. 236).

(To be continued.)